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TITLE: Effect of Inherited Breast Cancer Susceptibility on Treatment Outcomes After Conservative Surgery and

Radiation Therapy

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The presence of a mutation in a tumor suppressor gene, such as BRCA1, may have implications for patient management if patients with these mutations can be identified. Specifically, treatments such as breast conserving surgery and radiation therapy may be inappropriate if these patients are likely to be more susceptible to radiation-induced carcinogenesis or if they are more likely to recur locally in the breast because of multicentric disease. The performance period for this grant has recently been extended by one year to allow us to continue to accrue more patients. We have to date identified 192 eligible patients diagnosed with breast cancer at age 38 or younger and treated at the Joint Center for Radiation Therapy (JCRT) between 1987-96 of the 230 whom we expect to eventually contact. Patient accrual is steady and ongoing with 78 patients accrued to date. Lymphocytes from study subjects are being collected, immortalized and stored in liquid nitrogen. At the end of the collection period, testing for the presence of a germline BRCA1 mutation will be performed. Treatment outcome will then be compared between the groups of patients with and without mutations in BRCA1.					
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INTRODUCTION:

The presence of a germ line mutation in a tumor suppressor gene, such as BRCA1, may have implications for patient management if patients with these mutations can be identified. Specifically, treatments such as breast conserving surgery and radiation therapy may be inappropriate if these patients are likely to be more susceptible to radiation-induced carcinogenesis or if they are more likely to recur locally in the breast because of multicentric disease. This study will investigate the treatment outcomes after conservative surgery and radiation therapy among a cohort of young breast cancer patients who have BRCA1 mutations and a similarly-aged group who do not have mutations in BRCA1. The blood of young patients diagnosed with early-stage invasive breast cancer will be drawn and tested for the presence of mutations in the tumor suppressor gene BRCA1. At the end of three years, treatment outcomes will be compared between the patients in this group who have a mutation in the BRCA1 gene and those patients who do not. Blood will also be stored in order to test for mutations in other breast cancer susceptibility genes as such genes are identified and testing becomes available. A second objective will be to determine patient preferences regarding the optimal time to consider genetic testing for breast cancer susceptibility genes in this patient population. Since the results of testing may influence local treatment decisions. patient preferences for the timing of testing assume added importance.

BODY:

Methods: Recently the Performance Period was extended by one year from September 30, 2000 to September 30, 2001. This change has been approved by our grants officer. Thus this report is an annual report and not a final report.

We have to date identified 192 eligible patients diagnosed with breast cancer at age 38 or younger and treated at the Joint Center for Radiation Therapy at Harvard Medical School between 1987-96 of the 230 whom we expect to eventually contact. There remains a small group of patients (38) for whom address information and/or medical information is not easily available and this information is currently being gathered in hopes of reaching our target accrual goals.

To date, 78 patients have been accrued. This process is being ramped up with an increase in the number of letters sent out to patients per month.

Results: See above. No data has yet been generated from this study. There are currently no negative nor positive findings related to this project.

Progress related to statement-of-work:

Task 1	Months 1-6	Completed
Task 2	Months 1-6	Completed
Task 3	Months 3-24	In progress
Task 4	Months 6-24	In progress
Task 5	Months 6-30	In progress
Task 6	Months 6-36	In progress
Task 7	Months 24-34	Not yet initiated
Task 8	Months 30-33	Not yet initiated
Task 9	Months 33-36	Not yet initiated

KEY RESEARCH ACCOMPLISHMENTS: None to date, pending analysis.

REPORTABLE OUTCOMES:

-cell lines for 56 of the 78 accrued patients have been successfully immortalized and stored in liquid nitrogen.¹

CONCLUSIONS:

Currently we are on target to collect blood specimens for DNA analysis on all eligible patients. There are currently no positive nor negative findings from this project.

REFERENCES:

1. M. A. Anderson and J. F. Gusella, In Vitro 20, 856 (1984).